CLAIMS

1. Process for the synthesis of perindopril of formula (I):

$$H$$

$$CO_{2}H$$

$$H_{3}C$$

$$S)$$

$$CO_{2}Et$$

$$CO_{2}Et$$

$$CO_{3}Et$$

and pharmaceutically acceptable salts thereof,

5 characterised in that the compound of formula (II), of configuration (S):

$$CO_2R$$
 (II),

wherein R represents a hydrogen atom or a protecting group for the acid function,

is reacted with a compound of formula (III), of configuration (R):

wherein G represents a chlorine or bromine atom or a hydroxy, p-toluenesulphonyloxy, methanesulphonyloxy or trifluoromethanesulphonyloxy group,

in the presence of a base to yield the compound of formula (IV):

$$(S)$$
 CO_2R HN O (IV) , H_3C (R) G

wherein R and G are as defined hereinbefore,

which is subjected to an intramolecular coupling reaction to yield the compound of formula (V):

$$H_3C$$
 (S) (V) (R) (V)

wherein R and G are as defined hereinbefore,

which is reacted with the compound of formula (VI):

$$H_2N$$
 CO_2Et
 CH_3
 CO_2Et

to yield the compound of formula (VII):

wherein R is as defined hereinbefore,

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which is subjected to a catalytic hydrogenation reaction to yield, after deprotection where appropriate, the compound of formula (I).

- 2. Synthesis process according to claim 1, characterised in that R represents a benzyl or linear or branched (C₁-C₆)alkyl group.
- 5 3. Synthesis process according to claim 1, characterised in that the intramolecular coupling reaction is carried out either in the presence of a base and a catalyst based on palladium or using sodium hydride and copper(I) iodide or copper(I) bromide.
 - 4. Synthesis process according to claim 3, characterised in that the intramolecular coupling reaction is carried out in the presence of a base and a catalyst based on palladium and on an arylphosphine or bisphosphine.

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- 5. Synthesis process according to claim 4, characterised in that the base used for the intramolecular coupling reaction is selected from Cs₂CO₃, NaOtBu, Na₂CO₃, NaOAc and KOAc.
- 6. Synthesis process according to claim 4 or 5, characterised in that the catalyst based on palladium and on an arylphosphine or bisphosphine is selected from Pd(0)/PPh₃, Pd(0)/P(o-tolyl)₃, Pd(0)/P(1-naphthyl)₃, Pd(0)/P(o-methoxyphenyl)₃, Pd₂(dba)₃/P(o-tolyl)₃, Pd₂(dba)₃/P(1-naphthyl)₃, Pd₂(dba)₃/P(o-methoxyphenyl)₃, Pd₂(dba)₃/P(2-furyl)₃, Pd₂(dba)₃/dppp, Pd₂(dba)₃/(±)-BINAP and (DPPF)PdCl₂.CH₂Cl₂/DPPF,
- BINAP being understood to be 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, dba being understood to be dibenzylideneacetone,

 DPPF being understood to be 1,1'-bis(diphenylphosphino)ferrocene and dppp being understood to be 1,3-bis(diphenylphosphino)propane.
- Synthesis process according to claim 1, characterised in that G represents a chlorine or
 bromine atom or a p-toluenesulphonyloxy, methanesulphonyloxy or trifluoro-methanesulphonyloxy group.

- 8. Synthesis process according to claim 7, characterised in that the reaction between the compounds of formulae (V) and (VI) is carried out in the presence of an organic amine selected from triethylamine, pyridine and diisopropylethylamine or a mineral base selected from Na₂CO₃, K₂CO₃, NaHCO₃ and KHCO₃.
- 5 9. Synthesis process according to claim 1, characterised in that G represents a hydroxy group.
 - 10. Synthesis process according to claim 9, characterised in that the reaction between the compounds of formulae (V) and (VI) is carried out in the presence of N-methyl-N-phenyl-aminotriphenylphosphonium iodide or, when R is other than a hydrogen atom, by a Mitsunobu reaction.
 - 11. Compound of formula (IV):

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wherein R and G are as defined in claim 1.

12. Process according to any one of claims 1 to 10 for the synthesis of perindopril in the form of its tert-butylamine salt.